to expeditious development, evaluation, and marketing under 21 CFR part 312, subpart E.

(11) An explanation of how the data summarized and analyzed under paragraphs (b)(9) and (b)(10) of this section support the rationale for use of the drug in the rare disease or condition.

(12) A definition of the population from which subjects will be identified for clinical trials, if known.

(13) A detailed outline of any protocols under which the drug has been or is being studied for the rare disease or condition and a summary and analysis of any available data from such studies.

(14) The sponsor's proposal as to the scope of nonclinical and clinical investigations needed to establish the safety and effectiveness of the drug.

(15) Detailed protocols for each proposed United States or foreign clinical investigation, if available.

(16) Specific questions to be addressed by FDA in its recommendations for nonclinical laboratory studies and clinical investigations.

[57 FR 62085, Dec. 29, 1992; 58 FR 6167, Jan. 26, 1993]

§ 316.12 Providing written recommendations.

(a) FDA will provide the sponsor with written recommendations concerning the nonclinical laboratory studies and clinical investigations necessary for approval of a marketing application if none of the reasons described in § 316.14 for refusing to do so applies.

(b) When a sponsor seeks written recommendations at a stage of drug development at which advice on any clinical investigations, or on particular investigations would be premature, FDA's response may be limited to written recommendations concerning only nonclinical laboratory studies, or only certain of the clinical studies (e.g., Phase 1 studies as described in § 312.21 of this chapter). Prior to providing written recommendations for the clinical investigations required to achieve marketing approval, FDA may require that the results of the nonclinical laboratory studies or completed early clinical studies be submitted to FDA for agency review.

§ 316.14 Refusal to provide written recommendations.

(a) FDA may refuse to provide written recommendations concerning the nonclinical laboratory studies and clinical investigations necessary for approval of a marketing application for any of the following reasons:

(1) The information required to be submitted by § 316.10(b) has not been submitted, or the information submitted is incomplete.

(2) There is insufficient information about:

(i) The drug to identify the active moiety and its physical and chemical properties, if these characteristics can be determined; or

(ii) The disease or condition to determine that the disease or condition is rare in the United States; or

(iii) The reasons for believing that the drug may be useful for treating the rare disease or condition with that drug; or

(iv) The regulatory and marketing history of the drug to determine the scope and type of investigations that have already been conducted on the drug for the rare disease or condition; or

(v) The plan of study for establishing the safety and effectiveness of the drug for treatment of the rare disease or condition.

(3) The specific questions for which the sponsor seeks the advice of the agency are unclear or are not sufficiently specific.

(4) On the basis of the information submitted and on other information available to the agency, FDA determines that the disease or condition for which the drug is intended is not rare in the United States.

(5) On the basis of the information submitted and on other information available to the agency, FDA determines that there is an inadequate basis for permitting investigational use of the drug under part 312 of this chapter for the rare disease or condition.

(6) The request for information contains an untrue statement of material fact.

(b) A refusal to provide written recommendations will be in writing and will include a statement of the reason for FDA's refusal. Where practicable,

FDA will describe the information or material it requires or the conditions the sponsor must meet for FDA to provide recommendations.

(c) Within 90 days after the date of a letter from FDA requesting additional information or material or setting forth the conditions that the sponsor is asked to meet, the sponsor shall either:

(1) Provide the information or material or amend the request for written recommendations to meet the conditions sought by FDA; or

(2) Withdraw the request for written recommendations. FDA will consider a sponsor's failure to respond within 90 days to an FDA letter requesting information or material or setting forth conditions to be met to be a withdrawal of the request for written recommendations.

Subpart C—Designation of an Orphan Drug

§ 316.20 Content and format of a request for orphan-drug designation.

(a) A sponsor that submits a request for orphan-drug designation of a drug for a specified rare disease or condition shall submit each request in the form and containing the information required in paragraph (b) of this section. A sponsor may request orphan-drug designation of a previously unapproved drug, or of a new orphan indication for an already marketed drug. In addition, a sponsor of a drug that is otherwise the same drug as an already approved orphan drug may seek and obtain orphan-drug designation for the subsequent drug for the same rare disease or condition if it can present a plausible hypothesis that its drug may be clinically superior to the first drug. More than one sponsor may receive orphan-drug designation of the same drug for the same rare disease or condition, but each sponsor seeking orphan-drug designation must file a complete request for designation as provided in paragraph (b) of this section.

(b) A sponsor shall submit two copies of a completed, dated, and signed request for designation that contains the following:

(1) A statement that the sponsor requests orphan-drug designation for a rare disease or condition, which shall be identified with specificity.

(2) The name and address of the sponsor; the name of the sponsor's primary contact person and/or resident agent including title, address, and telephone number; the generic and trade name, if any, of the drug or drug product; and the name and address of the source of the drug if it is not manufactured by the sponsor.

(3) A description of the rare disease or condition for which the drug is being or will be investigated, the proposed indication or indications for use of the drug, and the reasons why such therapy is needed.

(4) A description of the drug and a discussion of the scientific rationale for the use of the drug for the rare disease or condition, including all data from nonclinical laboratory studies, clinical investigations, and other relevant data that are available to the sponsor, whether positive, negative, or inconclusive. Copies of pertinent unpublished and published papers are also required.

(5) Where the sponsor of a drug that is otherwise the same drug as an already-approved orphan drug seeks orphan-drug designation for the subsequent drug for the same rare disease or condition, an explanation of why the proposed variation may be clinically superior to the first drug.

(6) Where a drug is under development for only a subset of persons with a particular disease or condition, a demonstration that the subset is medically plausible.

(7) A summary of the regulatory status and marketing history of the drug in the United States and in foreign countries, e.g., IND and marketing application status and dispositions, what uses are under investigation and in what countries; for what indication is the drug approved in foreign countries; what adverse regulatory actions have been taken against the drug in any country.

(8) Documentation, with appended authoritative references, to demonstrate that:

(i) The disease or condition for which the drug is intended affects fewer than 200,000 people in the United States or, if the drug is a vaccine, diagnostic